

## Clinical implications of atrial isomerism

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**SUMMARY** Right atrial isomerism or left atrial isomerism is frequently diagnosed as situs ambiguous without further discrimination of the specific morbid anatomy. Thirty six cases of right atrial isomerism and seven cases of left atrial isomerism were collected from the records and pathological museum at the National Taiwan University Hospital. There was a necropsy report for 18 cases. In all patients one or more of the following conditions was met: (a) isomeric bronchial anatomy, (b) echocardiographic and angiographic evidence of isomerism, and (c) surgical or necropsy evidence of abnormal atrial anatomy. An anomalous pulmonary venous connection was present in 55% of patients with right atrial isomerism; in left atrial isomerism one case (14%) had a partial anomalous pulmonary venous connection. Forty per cent of cases of anomalous pulmonary venous connection with right atrial isomerism had obstruction. Six (86%) of seven cases with left atrial isomerism had an ambiguous biventricular atrioventricular connection. In contrast, univentricular atrioventricular connection (26 of 36, 72%) was significantly more common in right atrial isomerism. A common atrioventricular valve was the most frequent mode of connection in both forms. Two discrete atrioventricular valves were significantly more common in left atrial isomerism. Atrioventricular valve regurgitation was detected in 14 cases. Double outlet right ventricle was the most common type of ventriculoarterial connection. The most commonly cited causes of death after either palliative or definitive operation were undetected anomalous pulmonary venous connection, pulmonary venous stricture, and uncorrected atrioventricular valve or aortic regurgitation complicated by abnormal coagulation.

Although the prognosis is poor, successful operation depends on knowledge of the precise anatomical arrangement associated with atrial isomerism.

Complex congenital heart disease is known to be combined frequently with visceral heterotaxia,<sup>1,2</sup> and until recently the emphasis has been on arrangement of abdominal organs and presence or absence of spleen.<sup>1-6</sup> The concept of asplenia and polysplenia syndromes in association with bilateral right sidedness and left sidedness has led to great confusion and misunderstanding. It is recognised that there is less discord between the arrangement of atria and thoracic organs than that between atria and abdominal organs.<sup>7,8</sup> The pattern of lung lobulation is less accurate than the bronchial arrangement in predicting atrial situs.<sup>7,8</sup> Thus right atrial isomerism is not always associated with asplenia nor left atrial isomerism with polysplenia.

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Accepted for publication 19 November 1987

We have studied patients with atrial isomerism in our hospital to get a better understanding of the anatomical arrangement, so that operations may be better planned.

### Patients and methods

We reviewed the records of paediatric and surgical patients at the National Taiwan University Hospital from November 1983 to November 1986 and all the available heart specimens in the pathology department. Every study patient met one or more of the following criteria: (a) isomeric bronchial anatomy shown by penetrating chest radiographs or high kilovoltage filter film; (b) echocardiographic and angiographic evidence of atrial isomerism; and (c) surgical or necropsy evidence of atrial morphology. Cross sectional echocardiography was performed in 33 patients. There were 18 necropsy specimens. All chest radiographs and angiograms

were reviewed. We studied the position of the heart and its apex; the air-bronchogram; anomalies of systemic and pulmonary venous connection, atrioventricular connection, and ventriculoarterial connection; and the presence or absence of Howell-Jolly bodies. The criterion for establishing right atrial isomerism is the presence of bilateral triangular right atrial appendages or early branching of the bronchus.<sup>7,8</sup> In left atrial isomerism there are bilateral slender left atrial appendages or hypoarterial and longer bronchi. We used methods of sequential segmental analysis and nomenclature used elsewhere.<sup>7,9</sup> The statistical significance of the differences between two groups was evaluated by a Fischer's exact test. In all analyses, the 95% confidence level was regarded as significant.

## Results

There were seven cases (4 female, 3 male) of left atrial isomerism and 36 cases of right atrial isomerism (15 female and 21 male).



Fig 1 Anomalous left upper pulmonary vein (white arrow head) draining into left superior vena cava (star) in a case of right atrial isomerism with modified Blalock-Taussig shunt (arrow).

## SYSTEMIC VENOUS CONNECTION

Interruption of inferior vena cava was seen in four (59%) cases of left atrial isomerism. Bilateral inferior vena cava was found in two cases of right atrial isomerism. Sixteen cases (44%) of right isomerism had bilateral superior vena cava. In 20 with single superior vena cava the vein was right sided in 13 and left sided in seven.

## PULMONARY VENOUS CONNECTION

One partial anomalous pulmonary venous connection (14%) was found in left atrial isomerism. In patients with right atrial isomerism, eight (22%) had partial anomalous pulmonary venous connection and 12 (33%) had total anomalous pulmonary venous connection. A left upper pulmonary vein draining into left superior vena cava was most frequently seen in partial anomalous pulmonary venous connection (fig 1). In one case the right upper pulmonary vein was hypoplastic and a membrane covered the orifice of right lower pulmonary vein at its entry into the right sided morphologically right atrium (fig 2a). Oedema developed in the right upper lung field after a modified Blalock-Taussig Shunt (fig 2b). Total anomalous extracardiac connection was to the superior vena cava in three, to an infradiaphragmatic channel in three, and in two cases it was of a mixed type. The other five cases of total anomalous pulmonary venous connection drained to the heart through a narrow channel of pulmonary venous confluence (fig 3). In one case of total anomalous pulmonary venous connection the ascending vein was trapped inside the lung parenchyma and drained to the superior vena cava, which was obstructed by a stricture. There was clinically significant obstruction in eight (40%) of the 20 cases of partial or total anomalous pulmonary venous connection with right atrial isomerism.

## ATRIAL SEPTUM

A common atrium was found in 29 cases: four with left isomerism and 25 with right isomerism. A strand of atrial septal remnant was the most common feature. If present the oval fossa located in the superior rim of atrial septum was hypoplastic. In one case of right atrial isomerism unroofing of coronary sinus had produced a small interatrial communication. A sinus septum (left venous valve or septum spurium) was the only intra-atrial septum present in three cases of right atrial isomerism.

## ATRIOVENTRICULAR CONNECTION (TABLE 1)

In atrial isomerism the biventricular atrioventricular connection is neither concordant nor discordant. It is ambiguous. A biventricular and ambiguous connection was common in left atrial isomerism (86%), whereas a univentricular atrioventricular connection

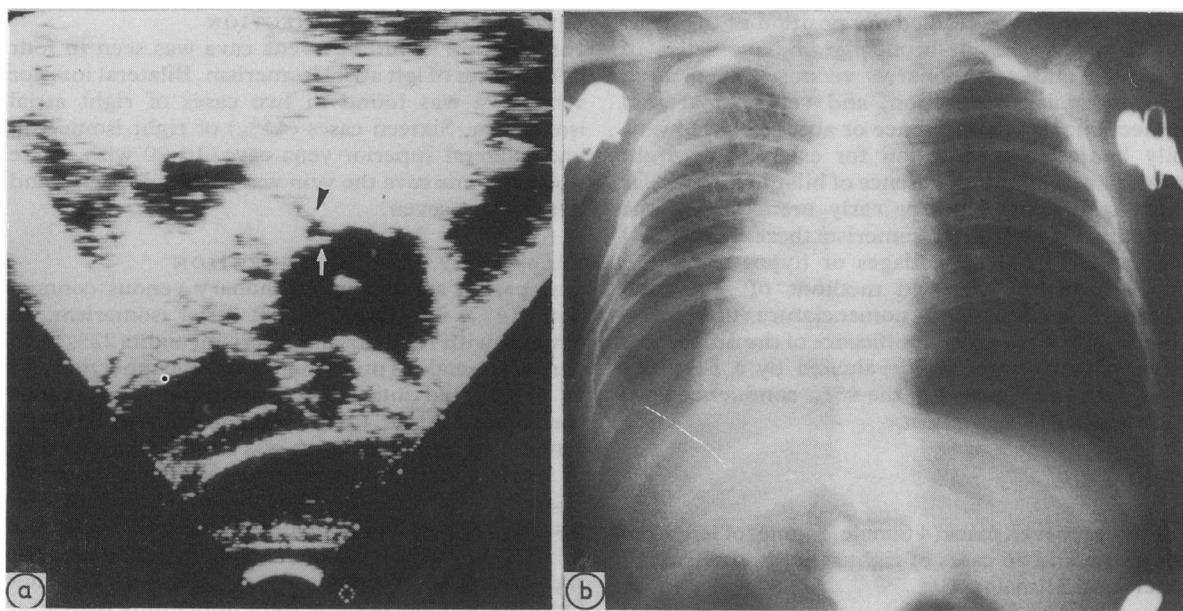


Fig 2 (a) Echocardiogram of a hypoplastic right upper pulmonary vein (black arrow head) in a case of right atrial isomerism. The entry site of right upper pulmonary vein is partially obstructed by a membrane (arrow). (b) Chest x ray showing lung oedema in the right upper lung field after a modified Blalock-Taussig shunt.

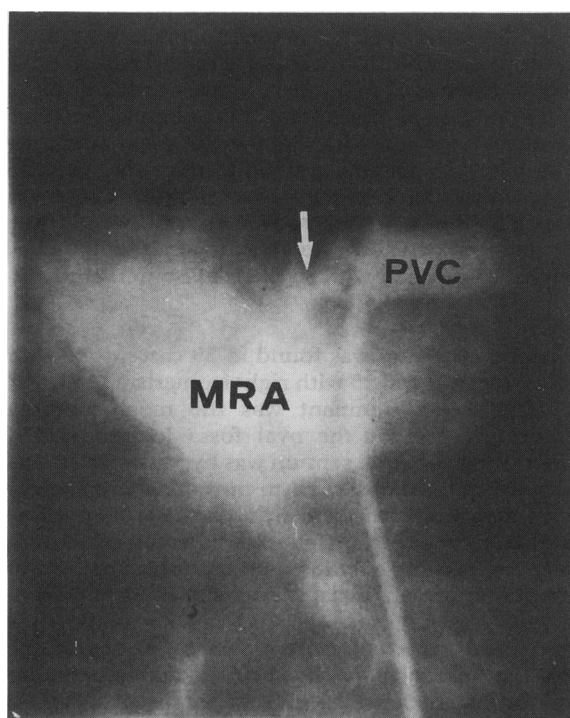


Fig 3 Angiogram showing the pulmonary venous confluence (PVC) draining into the morphologically right atrium (MRA) through a narrow channel (arrow) in a case of right atrial isomerism. This patient survived the Fontan operation after relief of pulmonary venous obstruction.

was common in right atrial isomerism (72%) ( $p < 0.005$ ) (table 1). There was a common atrioventricular valve in 36 (84%) of the 43 cases. None of the cases with univentricular atrioventricular connections had two atrioventricular valves. Two discrete atrioventricular valves were present in four of seven cases with left atrial isomerism. This feature was less common in right atrial isomerism (three (9%) of 36) ( $p < 0.005$ ). There was atrioventricular valve regurgitation in four cases of left atrial isomerism and 10 cases of right atrial isomerism. Valvar regurgitation was more frequent with a common atrioventricular valve than two atrioventricular valves (NS).

#### VENTRICULOARTERIAL CONNECTION

Discordant connection and double outlet right ventricle were common in right atrial isomerism (table 2). There was pulmonary obstruction in 29 (81%)

Table 1 Type and mode of atrioventricular connection in 43 patients with atrial isomerism

Isomerism		Ambiguous biventricular	Univentricular		
			Left	Right	Indeterminate
Left	7	6	1	0	0
Right	36	10	11	14	1
n = 43		2 valve	1 valve	2 valve	1 valve
Left	7	4 (2)*	2 (2)*	0	1
Right	36	3	7 (4)*	0	26 (6)*

\*Regurgitation.

Table 2 Type of ventriculoarterial connection in 43 patients with atrial isomerism

Isomerism (n = 43)		Concordant		Discordant		DORV		DOV		Single	
AV connection		B	U	B	U	B	U	B	U	B	U
Left	7	2	0	0	0	4	0	0	0	0	1
Right	36	0	0	1	9	4	12	0	1	5	4

B, biventricular; DORV, double outlet right ventricle; DOV, double outlet ventricle; U, univentricular.

cases of right atrial isomerism and five (71%) cases of left atrial isomerism. Nine (25%) cases of right atrial isomerism and one (14%) of left atrial isomerism had pulmonary atresia.

#### CARDIAC POSITION AND DIRECTION OF THE APEX

The cardiac apex was directed to the left in five (71%) cases of left atrial isomerism and in 26 (72%) cases of right atrial isomerism. It was directed to the right in nine (25%) cases of right atrial isomerism and in two (29%) cases of left atrial isomerism. One case of right atrial isomerism had a midline heart with the apex directed to the middle.

#### BRONCHIAL ARRANGEMENT

The bronchial arrangement was determined by x ray and necropsy (if available) in 34 patients. In nine patients radiographs were unsatisfactory and there was no necropsy report. There was no discord between the atrial situs and the bronchial arrangement.

#### ARRANGEMENT OF THE ABDOMINAL ORGANS

Normal arrangement (solitus) was found in three patients with right atrial isomerism and mirror image arrangement (inversus), in two with right atrial isomerism, and in one with left atrial isomerism. The remaining cases had heterotaxy. Two cases of hiatus hernia and one case of inguinal hernia were associated with right atrial isomerism. Omphalocele was found in one case of left atrial isomerism. A Howell-Jolly body was not found in seven (19%) cases of right atrial isomerism.

#### SURVIVAL IN THE UNOPERATED GROUP

No operation was performed for cardiac anomalies in 10 patients with right atrial isomerism and three with left atrial isomerism. Two patients with right atrial isomerism aged 2 months and 6 years and two with left atrial isomerism aged 3 and 8 months were known to be alive at the end of November 1986. Their age was 2 month and 6 year respectively. The mean (SE) age at death in eight unoperated cases of right atrial isomerism was 80 (44) days. The surviving patients are either awaiting a suitable time for operation or are not suitable for operation.

#### SURGERY AND ITS RESULTS

Thirty patients were referred for cardiovascular surgery—26 with right atrial isomerism and four with left atrial isomerism. One patient with left atrial isomerism died after omphalocele repair. Ten patients with right atrial isomerism had systemic to pulmonary shunts (Blalock-Taussig, Gortex shunt, or central shunt); six died (60%). Two patients with left atrial isomerism and a Gortex shunt have survived. Seven patients with right atrial isomerism and one patient with left atrial isomerism had a Fontan operation; only one patient survived. Pulmonary artery banding was attempted in three patients with right isomerism; all of them died. Two patients with right atrial isomerism had atrioventricular valve replacement for regurgitation; one survived. The other case of right atrial isomerism survived the repair of an unroofed coronary sinus. Two patients underwent cardiopulmonary bypass to correct total anomalous pulmonary venous connection; both died. One patient each in two groups had a Rastelli operation; both died.

#### CAUSES OF DEATH AFTER SURGERY (TABLES 3 AND 4)

The main causes of death after Fontan operation (table 3) were consequences of residual anomalous pulmonary venous connections, atrioventricular valve regurgitation, aortic regurgitation, or a ductus arteriosus, which resulted in cardiac failure. A bleeding complication occurred in two patients within a week of a Fontan operation although the central venous pressure was maintained around 18 mm Hg. Anomalous pulmonary venous connection could be

Table 3 Causes of death after Fontan operation (n = 7)

Cause	No
Sepsis	1
PAPVC	2
Coagulopathy*	2
Residual ASD	1
Pump failure	1

\*One patient also had aortic regurgitation.

ASD, atrial septal defect; PAPVC, partial anomalous pulmonary venous connection.

Table 4 Causes of death after shunt operation ( $n = 6$ )

Cause	No
PAPVC	1
TAPVC	3
Pulmonary vein stricture and PAPVC	1
Shunt obliterated plus PAPVC	1

PAPVC, partial anomalous pulmonary venous connection; TAPVC, total anomalous pulmonary venous connection.

seen in all patients who died after shunt operation (table 4).

## Discussion

Right atrial isomerism is characterised by bilateral triangular, morphologically right atrial, appendages, both joining the atrial chamber along a broad front with internal terminal crest. In left atrial isomerism there is a bilateral small finger-shaped morphologically left atrial appendage joining the atrial chamber along a narrow front without an internal terminal crest.<sup>7</sup> In life atrial situs is best diagnosed by examination of bronchial anatomy on a high kilovoltage filter chest radiograph.<sup>8,10</sup> Like Deanfield *et al* we found that an anteroposterior view gave the most informative air bronchogram.<sup>8</sup> Examination at operation and necropsy in our series confirmed that there was no discord between the atrial situs and the bronchial situs, although others have reported inappropriate bronchial arrangements.<sup>8,11</sup> The absence of spleen in so-called asplenia syndrome should invariably be accompanied by a Howell-Jolly body, but this was not present in 19% of our patients with right atrial isomerism. Use of the Howell-Jolly body as a diagnostic predictor for right atrial isomerism would have missed a fifth of these cases.

Echocardiography of the abdominal great vessels and hepatic venous drainage are diagnostically more accurate than an assessment of the abdominal organs.<sup>11,12</sup> One of our patients with right atrial isomerism, however, had the usual arrangement of both abdominal organs and great vessels.

As in other clinical and pathological series we found that the pulmonary venous connection was abnormal in 55% of patients with right atrial isomerism.<sup>11</sup> The high frequency (97%) of anomalous pulmonary venous connection in necropsy series<sup>7</sup> may be because those cases that come to necropsy die of severe associated abnormality. The poor results of definitive surgery or palliative shunts in our series may be related to the presence of anomalous pulmonary venous connection. In a recent series from

Brompton Hospital 10 patients with right isomerism had shunts; seven died.<sup>11</sup> Although the cause of death was not stated, these results suggest that babies with right atrial isomerism were too ill to stand even a shunt procedure. One factor may be that increased pulmonary blood flow through the shunt flooded the lung with pulmonary venous obstruction. Cross sectional echocardiography is the most informative investigation for anomalous pulmonary venous connection in right atrial isomerism.<sup>13</sup> Preoperative evaluation in patients with right atrial isomerism can be difficult because there are two morphologically right lungs which considerably reduce the size of the precordial echo-window.<sup>11</sup> In such cases, it is important to check the pulmonary venous drainage of upper lobe on both sides during operation. Sometimes the drainage orifice of middle lobe only is mistaken for the drainage orifice of both upper and middle lobes of bilateral right lungs. In our series two consecutive cases of anomalous pulmonary venous connection in which the left upper pulmonary vein ran into the left superior vena cava were not detected until necropsy.

Why is anomalous pulmonary venous connection so common in right atrial isomerism? The morphologically right atrium might reject the entry of pulmonary veins during embryogenesis, or the pulmonary veins might lose their ability to recognise and connect with the morphologically right atrial chamber. These two mechanisms could account for total anomalous pulmonary venous connection, partial anomalous pulmonary venous connection, hypoplastic pulmonary vein, and pulmonary venous confluence with a narrow entry into the atrial roof as found in almost all the patients with right atrial isomerism. The same mechanisms could account for the arrangement of the suprarenal portion of the inferior vena cava in left atrial isomerism. This could explain why an interrupted inferior vena cava was so common in our cases (57%) and those reported by others (64%).<sup>7</sup> The high incidence (39–64%) of partial anomalous pulmonary venous connection in left atrial isomerism in published reports<sup>2,7,11,14</sup> could be explained by recognition of pulmonary vein by the ipsilateral morphologically left atrium producing a bilateral connection. For the same reason the inferior vena cava might connect with the ipsilateral morphologically right atrium and produce bilateral inferior caval veins as we found in two cases of right atrial isomerism. This speculation is contradicted by the frequency of total anomalous pulmonary venous connection in left atrial isomerism (0–13%),<sup>11,14</sup> which is much lower than its occurrence in right atrial isomerism (38–97%).<sup>2,7,11</sup> An interrupted inferior vena cava is sporadically reported in right atrial isomerism.<sup>11</sup>

One of our cases of left atrial isomerism had omphalocele. Two cases of right isomerism had hiatus hernia and one inguinal hernia. The relevance of these abnormalities is unknown. Left atrial isomerism was less common in our series than in other series.<sup>11 15</sup> This might be because associated malformations are often less severe in this condition and would not lead to referral to a regional centre. So far the results of operation in babies and children with right atrial isomerism with anomalous pulmonary venous connection are not encouraging. The precise identification of the anatomical abnormality in cases of the atrial isomerism is a prerequisite for successful operation.

We thank Professor and Chairman Kai-Mo Chen, Department of Surgery, College of Medicine, National Taiwan University, for his constant support of our study and for revision of the paper.

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